

# Chapter 15

## The Importance of Energy Changes and Electron Transfer in Metabolism

### SUMMARY

#### Section 15.1

- Standard states are benchmark conditions chosen to have a basis of comparison for energy changes in processes under a wide variety of conditions.
- Free-energy changes under standard conditions can be related to free-energy changes under any condition by a well known equation.

#### Section 15.2

- The usual thermodynamic standard state implies that the system involved is at  $pH = 0$ , which is seldom, if ever, found in living things. The modified standard state explicitly states that the system is at  $pH = 7$ .

#### Section 15.3

- Metabolism is the sum total of the chemical reactions of biomolecules in an organism.

#### Section 15.4

- In catabolism, large molecules are broken down to smaller products, releasing energy and transferring electrons to acceptor molecules of various sorts. The overall process is one of oxidation.
- In anabolism, small molecules react to give rise to larger ones; this process requires energy and involves acceptance of electrons from a variety of donors. The overall process is one of reduction.

#### Section 15.5

- Two coenzymes, NADH and  $FADH_2$ , play a crucial role in biological oxidation-reduction reactions. Hydrogen ions are transferred in addition to electrons.

#### Section 15.6

- Hydrolysis of ATP to ADP releases energy.
- In the coupling of biochemical reactions, the energy released by one reaction, such as ATP hydrolysis, provides energy for another.

#### Section 15.7

- Metabolic pathways proceed in many stages, allowing for efficient use of energy.
- Many coenzymes, particularly coenzyme A (CoA) play a crucial role in metabolism.

## LECTURE NOTES

Thermodynamics is arguably the most difficult of topics discussed for students. Even though this will have been covered in a general chemistry course, the concepts remain a challenge. A useful strategy is to focus on importance of spontaneity for metabolic processes, and avoid getting bogged down in the mathematical underpinnings. The discussion of thermodynamics may take up to one lecture, dependent upon the depth of presentation. A second lecture will likely be devoted to fundamentals of oxidation-reduction reactions, their importance to biochemistry, and the mechanisms of coupling the production and use of energy.

## LECTURE OUTLINE

- I. Thermodynamics
  - A. Standard states
  - B. Free energy changes
  - C. Relationship between  $\Delta G^\circ$  and  $K_{eq}$
  - D. Modified standard state for biochemical usage
- II. Metabolism
  - A. Catabolism and anabolism
  - B. Oxidation-reduction reactions
    1. Oxidizing and reducing agents
    2. Half-reactions
  - C. Coenzymes in biological oxidation-reduction reactions
- III. Coupling of energy production and use
  - A. ATP and other organophosphates
  - B. State functions
  - C. Coupling of reactions
  - D. Use of coenzyme A as an example

## ANSWERS TO PROBLEMS

### 15.1 Standard States for Free-Energy Changes

1. There is a connection, and it is one of the most important points in this chapter. It can be expressed in the equation  $\Delta G^\circ = -RT \ln K_{eq}$ .
2. Reaction (a) would take place only if it is coupled to an exergonic reaction. Reaction (b) would proceed only if coupled to an exergonic reaction. Reaction (c) would proceed as written.
3. The information given here deals with the thermodynamics of the reaction, not the kinetics. It is not possible to predict the rate of the reaction.
4. The free-energy change can be used to predict the spontaneity of a reaction under conditions of constant temperature and pressure.
5. Many endergonic reactions are necessary for life processes. They need a source for the energy they require, and that source is the energy released by exergonic reactions.

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## 15.2 A Modified Standard State for Biochemical Applications

6. The usual thermodynamic standard state refers to  $\text{pH} = 0$ . This is not very useful in biochemistry.
7. Statement (a) is true, but statement (b) is not. The standard state of solutes is normally defined as unit activity ( $1\text{ M}$  for all but the most careful work). In biological systems, the  $\text{pH}$  is frequently in the neutral range (i.e.,  $\text{H}^+$  is close to  $10^{-7}\text{ M}$ ); the modification is a matter of convenience. Water is the solvent, not a solute, and its standard state is the pure liquid.
8. The designation  $\Delta G^{\circ\prime}$  indicates a biological standard state. If the prime is omitted, then it is for chemical standard states.
9. No, there is no relationship between the thermodynamic quantity  $\Delta G^{\circ}$  and the speed. The  $\Delta G^{\circ}$  reflects the thermodynamic possibility under standard states. Speed is a kinetic quantity that is based on the ability of an enzyme to catalyze the reaction and the real substrate concentrations in the cell.
10. Assuming one significant figure,  $20\text{ kJ mol}^{-1}$ ,  $0\text{ kJ mol}^{-1}$ ,  $+30\text{ kJ mol}^{-1}$ .
11.  $\Delta G^{\circ\prime} = \Delta H^{\circ\prime} - T\Delta S^{\circ\prime}$  and  $\Delta S^{\circ\prime} = 34.9\text{ J mol}^{-1}\text{ K}^{-1} = 8.39\text{ cal mol}^{-1}\text{ K}^{-1}$ . There are two particles on the reactant side of the equation and three on the product side, representing an increase in disorder.
12. Assuming 298 K and one significant figure:
  - (a)  $-50\text{ kJ}$
  - (b)  $-20\text{ kJ}$
  - (c)  $-20\text{ kJ}$
13. The levels of substrates and products can affect the true  $\Delta G$  of a reaction, changing it from zero to a high number as in part (a).  $\Delta G$  is negative when there is a larger amount of substrate than product.
14. The overall  $\Delta G^{\circ\prime} = -260.4\text{ kJ mol}^{-1}$  or  $-62.3\text{ kcal mol}^{-1}$ . The reaction is exergonic, because it has a large, negative  $\Delta G^{\circ\prime}$ .
15. Greater than 3333 to 1.
16. Reaction (a) will not proceed as written;  $\Delta G^{\circ\prime} = +12.6\text{ kJ}$ . Reaction (b) will proceed as written;  $\Delta G^{\circ\prime} = -20.8\text{ kJ}$ . Reaction (c) will not proceed as written;  $\Delta G^{\circ\prime} = +31.4\text{ kJ}$ . Reaction (d) will proceed as written;  $\Delta G^{\circ\prime} = -18.0\text{ kJ}$ .
17. Yes, *if* you correct for the difference in temperature and concentrations from the standard values.
18. Two aspects are involved here. (a) Very rarely, if ever, are *in vivo* concentrations standard concentrations; actual  $\Delta G$  (not  $\Delta G^{\circ}$ ) values are very dependent on local concentrations, especially if the number of reactant molecules and product molecules is not the same. (b) Values of  $\Delta G^{\circ}$  rigorously apply only to *closed* systems that can reach equilibrium. Biochemical systems, however, are *open* systems and do not reach equilibrium. If you were at equilibrium, you would be dead. Metabolic pathways involve series of reactions, and the metabolic pathways themselves are interconnected, including processes that take in materials from the surroundings and release waste products to the surroundings.

**15.3 The Nature of Metabolism**

19. Group 1: catabolism, oxidative, energy-yielding. Group 2: anabolism, reductive, energy-requiring.
20. The local decrease in entropy associated with living organisms is balanced by the increase in the entropy of the surroundings caused by their presence. Coupling of reactions leads to overall dispersal of energy in the Universe.
21. The synthesis of sugars by plants in photosynthesis is endergonic and requires light energy from the Sun.
22. The biosynthesis of proteins is endergonic and is accompanied by a large decrease in entropy.
23. The ATP constantly generated by living organisms is used as a source of chemical energy for endergonic processes. There is a good deal of turnover of molecules, but no net change.

**15.4 The Role of Oxidation and Reduction in Metabolism**

24.
  - (a) NADH is oxidized,  $\text{H}^+ + \text{NADH} \rightarrow \text{NAD}^+ + 2\text{e}^- + 2\text{H}^+$ . The aldehyde is reduced,  $\text{CH}_3\text{CH}_2\text{CHO} + 2\text{e}^- + 2\text{H}^+ \rightarrow \text{CH}_3\text{CH}_2\text{CH}_2\text{OH}$ .
  - (b)  $\text{Fe}^{2+}$  is oxidized,  $\text{Fe}^{2+} \rightarrow \text{Fe}^{3+} + \text{e}^-$ .  $\text{Cu}^{2+}$  is reduced,  $\text{Cu}^{2+} + \text{e}^- \rightarrow \text{Cu}^+$ .
25.
  - (a) The aldehyde is the oxidizing agent; NADH is the reducing agent.
  - (b)  $\text{Cu}^{2+}$  is the oxidizing agent;  $\text{Fe}^{2+}$  is the reducing agent.

**15.5 Coenzymes in Biologically Important Oxidation–Reduction Reactions**

26.  $\text{NAD}^+$ ,  $\text{NADP}^+$ , and FAD all contain an ADP moiety.
27. In NADPH, the 2' hydroxyl of the ribose attached to the adenine has a phosphate attached.
28. There is little effect in the reactions. Both are coenzymes involved in oxidation–reduction reactions. The presence of the phosphate distinguishes two separate pools of coenzymes so that different ratios of  $\text{NADPH}/\text{NADP}^+$  versus  $\text{NADH}/\text{NAD}^+$  can be maintained.
29.  $\text{NAD}^+$  is the oxidizing agent in reactions in which a nutrient is the substance to be oxidized. Like all oxidizing agents,  $\text{NAD}^+$  is reduced, producing NADH.
30. The oxidation of glucose to carbon dioxide and water takes place in many steps. This arrangement allows for use of the coenzymes involved and favors production of ATP.
31. None of these statements is true. Some coenzymes are involved in group-transfer reactions (recall this from Chapter 7). Many coenzymes contain phosphate groups, and CoA contains sulfur. ATP does not represent stored energy, but is generated on demand.
32. Redox reactions.  $\text{NAD}^+$ , or NADPH in an anabolic process, would likely be used. FAD probably would not be used because its free-energy change is too low.
33. The second half reaction (the one involving NADH) is that of oxidation; the first half reaction (the one involving  $\text{O}_2$ ) is that of reduction. The overall reaction is  $\frac{1}{2}\text{O}_2 + \text{NADH} + \text{H}^+ \rightarrow \text{H}_2\text{O} + \text{NAD}^+$ .  $\text{O}_2$  is the oxidizing agent and NADH is the reducing reagent.

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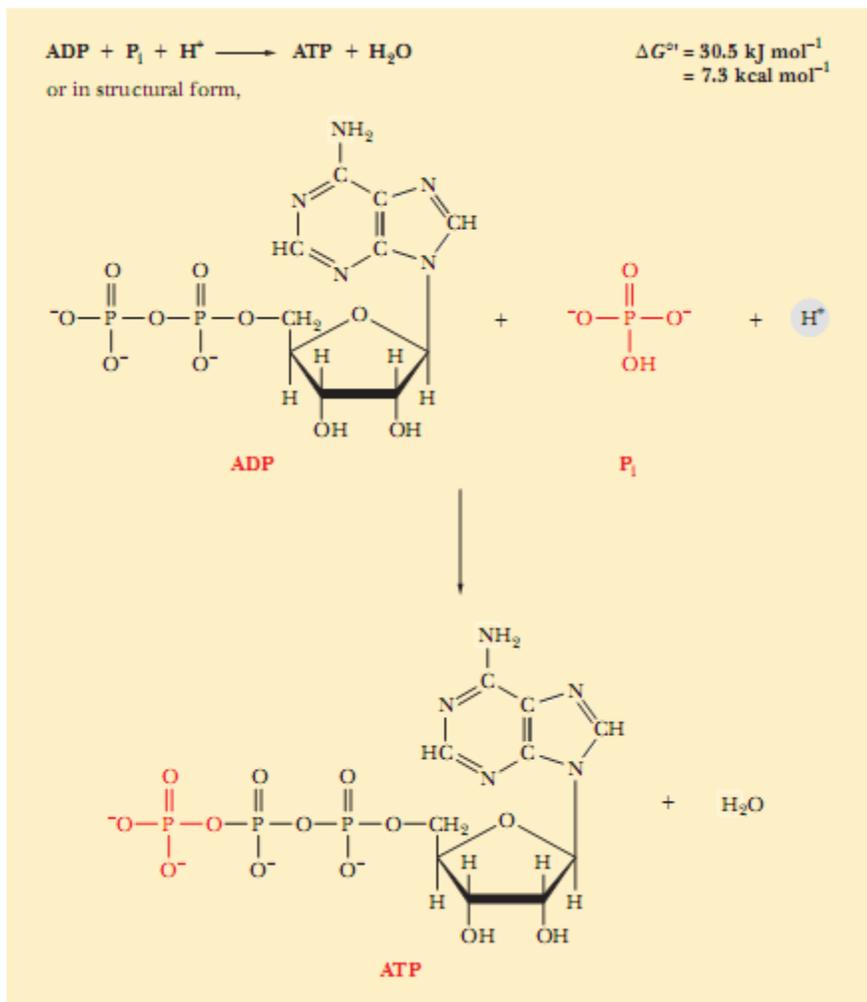
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34. See Figures 15.4 and 15.5.
35. Glucose-6-phosphate is oxidized, and  $\text{NADP}^+$  is reduced.  $\text{NADP}^+$  is the oxidizing agent, and glucose-6-phosphate is the reducing agent.
36. FAD is reduced, and succinate is oxidized. FAD is the oxidizing agent, and succinate is the reducing agent.
37. It is important to have two different pools of redox coenzymes. In the cytosol, the  $\text{NAD}^+/\text{NADH}$  ratio is high, but the  $\text{NADPH}/\text{NADP}^+$  ratio is also high. This means that anabolic reactions can take place in the cytosol, while catabolic reactions, such as glycolysis, can also take place. If there were not two different pools of these coenzymes, no single cell location could have both catabolism and anabolism. Having two different, but structurally related, reducing agents helps keep anabolic and catabolic reactions distinct from each other.
38. Only a portion of the energy released by exergonic reactions drives endergonic reactions. An example is the exergonic oxidation of glucose to two lactate ion), which releases 184.5 kilojoules for each mole of glucose. This reaction is coupled to the phosphorylation of two ADP to two ATP, an endergonic reaction that requires 61 kilojoules for each mole of glucose. The two amounts of energy are not the same.
39. Without the release of chemical energy in exergonic reactions, the endergonic reactions of metabolism, especially those of biosynthesis of DNA and proteins, could not take place.

## 15.6 Coupling of Production and Use of Energy

40. The ratio of substrates to products would have to be 321,258 to 1.
41. Creatine phosphate + ADP  $\rightarrow$  Creatine + ATP  
 $\Delta G^{\circ} = -12.6 \text{ kJ}$   
ATP + Glycerol  $\rightarrow$  ADP + Glycerol-3-phosphate  
 $\Delta G^{\circ} = -20.8 \text{ kJ}$
42. Glucose-1-phosphate  $\rightarrow$  Glucose +  $\text{P}_i$   
 $\Delta G^{\circ} = -20.9 \text{ kJ}$   
Glucose +  $\text{P}_i$   $\rightarrow$  Glucose-6-phosphate  
 $\Delta G^{\circ} = +12.5 \text{ kJ}$   
Glucose-1-phosphate  $\rightarrow$  Glucose-6-phosphate  
 $\Delta G^{\circ} = -8.4 \text{ kJ}$
43. In both pathways, the overall reaction is  $\text{ATP} + 2\text{H}_2\text{O} \rightarrow \text{AMP} + 2\text{P}_i$ . Thermodynamic parameters, such as energy, are additive. The overall energy is the same because the overall pathway is the same.
44. Phosphoarginine + ADP  $\rightarrow$  Arginine + ATP  
 $\Delta G^{\circ} = -1.7 \text{ kJ}$   
ATP +  $\text{H}_2\text{O} \rightarrow$  ADP +  $\text{P}_i$   
 $\Delta G^{\circ} = -30.5 \text{ kJ}$   
Phosphoarginine +  $\text{H}_2\text{O} \rightarrow$  Arginine +  $\text{P}_i$   
 $\Delta G^{\circ} = -32.2 \text{ kJ}$

45. ATP is less stable than ADP and  $P_i$  because of the charge distribution and loss of the resonance stabilization in the phosphate ion. There is stabilization (dispersal of energy) when ATP is hydrolyzed, leading to a negative free-energy change.



46. It is intermediate; thus, ATP is ideally positioned to serve as a phosphate donor or (as ADP) a phosphate acceptor, depending on local concentrations.
47. Creatine phosphate can phosphorylate ADP to ATP. There is a biochemical “germ of truth” here, but the effectiveness of such a supplement is another matter.
48. There is a large increase in entropy accompanying the hydrolysis of one molecule to five separate molecules.
49. PEP is a high-energy compound because energy is released upon its hydrolysis, owing to the resonance stabilization of the inorganic phosphate released and the possible keto–enol tautomerization of its product, pyruvate. See Figure 15.9.
50. The fact that a reaction is thermodynamically favorable does not mean that it will occur biologically. Even though there appears to be ample energy to catalyze the production of 2 ATPs from PEP, there is no enzyme that catalyzes this reaction.

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51. Sprints and similar short periods of exercise rely on anaerobic metabolism as a source of energy, producing lactic acid. Longer periods of exercise also draw on aerobic metabolism.

## 15.7 Coenzyme A in Activation of Metabolic Pathways

52. An activation step leads to an exergonic next step in a pathway. It is similar to the way in which organic chemists want to attach a good leaving group for the next step in a series of reactions.
53. Small energy changes generally involve mild conditions. Also, such reactions are more sensitive to relatively small changes in concentration and thus are easier to control.
54. Thioesters are high-energy compounds. The possible dissociation of the products after hydrolysis and resonance structures of the products facilitate reaction.
55. Coenzyme A serves several purposes. It is a high-energy compound, activating the initial steps of the metabolic pathway. It is used as a tag to “ earmark ” a molecule for a particular pathway. It is large and cannot cross membranes, so compartmentalization of pathways can be affected by binding metabolites to coenzyme A.
56. The size and complexity of the molecule make it more specific for particular enzyme-catalyzed reactions. In addition, it cannot cross membranes, so acyl-CoA molecules and other CoA derivatives can be segregated.